A Study Of

URETERIC STRICTURE IN GENITOURINARY TUBERCULOSIS

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CERTIFICATE

This is to certify that **Dr. K. SARAVANAN** bonafide student of M.Ch., Genitourinary Surgery (Branch IV), June 2003 to Feb. 2006 in The Department of Genitourinary Surgery Kilpauk Medical College, Chennai- 600 010, has done this dissertation on "**A STUDY OF URETERIC STRICTURE IN GENITOURINARY TUBERCULOSIS"** under my guidance and supervision in partial fulfillment of the regulations laid down by the Tamilnadu Dr.M.G.R. Medical University, Chennai, for M.Ch., Genitourinary Surgery (Branch IV), Examination to be held in February 2006.

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INTRODUCTION

Despite the fact that world has advanced remarkably in the past few decades, it is unfortunate that a disease, the causative organism which had been discovered more than a century ago, still continues its unrelentulous affliction, primarily of people already burdened by declining health standards prone to affection by various other diseases as well.

That, the divide between the advanced countries and the third world is still significant is exemplified by the fact that 38% of the global burden of tuberculosis occur in South East Asia. India accounts for nearly one third of global burden of tuberculosis.

There are about 16 to 20 million infectious cases of tuberculosis in the world with a yearly addition of 4 to 5 million new cases and with 3 million deaths each year. The magnitude of the problem was such that the WHO declared it as a global emergency in 1993.

With the use of powerful antimycobacterial drugs and formulation of effective chemotherapeutic regimens, the disease once considered untreatable is now considered curable but again,

the emergence of multi-drug resistant tubercle bacilli has compounded the problem since it is more associated with HIV infection.

Regrettably most of the infection occurs in the economically productive age group, commonly males. Poverty associated with poor nutrition and crowded living conditions represent the risk factors for the development of Tuberculosis.

Genitourinary Tuberculosis continues to be a significant clinical problem because of its nonspecific clinical presentation and variable radiological appearance.

Nearly 15 to 20% of all new cases of Tuberculosis involve sites outside of the lung, and approximately 30% of cases of extra pulmonary Tuberculosis involve the urogenital tract, therefore Genitourinary Tuberculosis makes approximately 5% of all cases of Tuberculosis.

The genitourinary tract is the second most common site for tuberculous infection after the lungs. The infection almost always affects the kidneys during the primary exposure to infection but does not manifest clinically.

The spread to the kidneys usually is hematogenous from the lungs, bone, or a GI tract focus. Genital tuberculosis is usually secondary to renal tuberculous infection.

Renal involvement may be indolent, with a latency period of more than 20 years after the primary infection to the appearance of urinary tract symptoms. In patients with renal tuberculosis, treatment involves antituberculous drugs, with surgical excision as an adjunct to antituberculous therapy.

The urine can be free of bacteria in less than 72 hours but anatomic changes can progress as part of the healing process.Genitourinary tuberculosis is primarily a disease of adults with a slight male predominance. The initial manifestations of Genitourinary tuberculosis occur most commonly in the 20 to 50 years age group.

Renal involvement is rare before the age of 20 years, and signs and symptoms are usually found before the age of 40 years.

The most common urinary symptoms are dysuria, frequency, nocturia, haematuria & flank pain. Less than 5% of patients with Genitourinary tuberculosis will have concomitant

active Pulmonary tuberculosis and 30 to 50% will have evidence of a lung abnormality on chest radiograph.

Mycobacterium Tuberculosis is the commonest causative organism.Renal tuberculosis typically progresses in two steps

1. Initial seeding

2.Reactivation

Diffuse haematogenous dissemination occurs at the time of initial pulmonary infection in approximately 25% of pulmonary cases. The bacilli are trapped in the periglomerular capillaries. If the host immunity is compromised, reactivation may occur between 5 and 25 years after the initial pulmonary infection.

Ureteral involvement, which is rarely found in the absence of more sever renal changes, mucosal nodules and ulceration occur with thickening of the ureteral wall, fibrosis and even calcification.

Renal damage secondary to ureteral strictures may be more severe than the effect of the original parenchymal involvement. The fibrosis causing the strictures represents healing of tuberculous ulcerations, and this may develop during appropriate chemotherapy.

Early scarring may be reversible by steroids therapy,but end-stage fibrotic strictures are irreversible.Dilatation and stenting of a ureteral stricture may regain or retain ureteral patency and salvage the kidney function but ureteral dynamics are often compromised.

Hence, the study of ureteric stricture due to genitourinary tuberculosis may throw a light into this complex problem,and better understanding of the disease and management.

AIM OF THE STUDY

1. To estimate the prevalence of ureteric involvement in Genitourinary Tuberculosis in the population served by this hospital.

2. To discuss the various modes of presentations of ureteric involvement in Genitourinary Tuberculosis.

3. To determine the significance of relevant laboratory investigations in the diagnosis.

4. To compare the efficacy of various therapeutic modalities adapted.

5. To asses the impact on morbidity and mortality of Genitourinary tuberculosis.

6. To draw diagnostic and therapeutic protocols for systematic approach towards a case of Ureteric Tuberculosis.

REVIEW OF LITERATURE

Tuberculosis is an acute on chronic infectious disease. It is usually caused by Mycobacterium Tuberculosis.

Mycobacterium bovis, Mycobacterium kansasii, and Mycobacterium intracellulare are rare causes of tuberculosis.

Mycobacterium customarily gains access to human body by inhalation, although the bovine organisms may be acquired by ingestion of unpasteurized milk. After initiation of the tuberculous infection, a primary pathologic focus develops, which usually heals spontaneously.

In addition, the primary infection often results in an initial silent bacillemia that is responsible for systemic spread of Mycobacterium with latent infection of many organs.

These latent foci of tuberculous infection may break down and result in overt tuberculosis of the kidney or other organs many years later. Bacillemia and seeding of the kidneys may occur from a focus of progressive primary or reactivation tuberculosis in other organs. Therefore any individual who has previously been infected with tuberculosis is at risk for developing renal involvement.

Renal infection is among the most common sites for extrapulmonary tuberculosis. It is uncommon for pulmonary tuberculosis to be active at the time of diagnosis of renal tuberculosis. Prevalence of pulmonary tuberculosis, the frequency of renal tuberculosis has not declined significantly in recent decades.

PATHOLOGY & PATHOGENESIS

In the haematogenous phase that takes place after the primary infection, both kidneys are seeded with tubercle bacilli in 90% of cases. However, clinically apparent renal tuberculosis is usually unilateral.

The initial lesions involve the renal cortex with multiple small granulomas in the glomeruli and in the juxtaglomerular regions. With patients in whom acquired cellular immunity develops, there is inhibition of bacterial multiplication and containment of the disease process to the renal cortex.

Microscopic examination reveals central caseation necrosis surrounded by pink staining epithelial histiocytes, Langhan's giant cells, and more peripherally lymphocytes and plasma cells. Most patients are asymptomatic and have normal findings on radiologic examination.

The asymptomatic cortical disease may be stable for many years and an incidental finding at Nephrectomy or autopsy. These early lesions may resolve completely either spontaneously or as a result of treatment. In untreated patients who fail to heal spontaneously, the lesions may progress slowly and remain asymptomatic for variable periods.

In most individuals, the latent period between initial exposure and reactivation of renal disease is 10 to 40 years. The cortical areas of infection may seed the glomerular filtrate, creating lesions in the tubules and Henle's loop, resulting in additional foci in the renal pyramid.

As the lesions progress, they produce areas of caseous necrosis, chronic interstitial nephritis with papillary necrosis, and parenchymal cavitation. Large blood vessels may show obliterative endarteritis.

Once cavities form, spontaneous healing is rare and destructive lesions result. Extensive peripelvic fibrosis may cause a substantial decrease in the pelvic capacity.

With extensive renal tuberculosis, parenchymal calcification is often present, varying from faint punctuate foci to

a complete cast of the kidney. Total destruction of the kidney may occur, resulting in autonephrectomy.

URETERAL TUBERCULOSIS

In ureteral tuberculosis, which is rarely found in the absence of more severe renal changes, mucosal nodules and ulceration occur with thickening of the ureteral wall, fibrosis, and even calcification.

Although ureteral tuberculosis develops mainly from a renal focus that ruptures into a calyx producing tuberculous bacilluria, other mechanisms are theoretically possible.

Such as the passage of tuberculous bacilli via communicating blood vessels and lymphatics from the renal parenchyma to the ureteral wall; direct extension of extramural lesions; reflux of infected urine into opposite ureter; and primary tuberculosis of the ureter without renal involvement.

Dilatation and a irregular appearance of the urothelium are the first signs of ureteral tuberculosis. These early changes occur most commonly in the distal ureter.

Although dilatations of the urinary tract in tuberculosis are commonly related to fibrotic strictures, an early and potentially

reversible dilatation has been attributed to spasm or mucosal edema at the terminal portion of the ureter.

The ureter is dilated initially but later it becomes strictured and eventually forms a straight, rigid tube. Ureteral strictures have been reported in about 10 to 20% of patients with renal tuberculosis. This process of destruction followed by fibrotic healing causes the characterstic beaded, corkscrew, or pipestem appearance of the ureter.

Multiple strictures are common in tuberculosis. Vesicoureteral reflux is commonly associated with ureteral tuberculosis due to involvement of the ureterovesical junction causing gaping ureteric orifice.

Edema of the trigonal mucosa can cause ureteral obstruction.Fibrosis in the region of the trigone may produce gaping of a ureteral orifice and vesicoureteral reflux.

Thickening of the renal pelvis or ureter is highly suggestive of tuberculosis. The fibrosis causing the strictures represents healing of tuberculous ulcerations, and this may develop during appropriate chemotherapy.

Early scarring may be reversible by steroid therapy, but end stage fibrotic strictures are irreversible.

Tubercles may involve the transitional epithelium, causing mucosal granulomas that project into the ureteric lumen.

Usually, the upper and/or lower third of the ureter is commonly involved.Stricture is more common in the lower third of ureter. Stricture involving the middle third is least common.

The vesicoureteric junction may become fixed and patulous, allowing vesicoureteric reflux. The kidneys are always involved when ureteric tuberculosis is present.

Bladder tuberculosis

Bladder tuberculous infection is almost always secondary to renal involvement. Initially, interstitial cystitis occurs, eventually causing bladder mucosal ulceration and thickening of the bladder wall.

End-stage disease causes scarring and bladder fibrosis, resulting in diminished capacity of the urinary bladder.

Bladder wall calcification is uncommon. Bladder tuberculosis may be complicated by fistulae or sinus tract formation, although these complications are rare.

Genital tuberculosis

Tuberculosis of the seminal vesicles usually occurs as a result of hematogenous spread. Descending infection is unusual. The pathologic process which occurs in the bladder (i.e., mucosal tuberculomas, ulceration, and fibrosis) also occurs in seminal vesicles. Calcification is present in only 10% of patients.

Unlike seminal vesicle tuberculosis, tuberculosis of the prostate is usually secondary to descending infection from the kidney. However, the kidneys may occasionally appear normal, suggesting subclinical infection or a hematogenous prostatic infection.

The tuberculous cavities or abscesses may discharge into the surrounding tissues forming sinuses or fistulae to the perineum or rectum, eventually resulting in a watering-can perineum.

Rarely the scrotum and urethra may be involved. Urethral involvement may be complicated by urethral strictures.

Tuberculosis may cause chronic epididymitis and epididymo-orchitis. Tuberculous granulomas may develop within the testes and epididymis and rarely may be complicated by abscesses and discharging sinuses. Thickening of the scrotal wall and tunica albuginea and moderate hydrocele also may be observed occasionally.

Female genital tuberculosis is invariably secondary to tuberculosis elsewhere, and spread may be hematogenous, via the lymphatic system, or by direct spread from adjacent organs.

Patients usually present with infertility, menstrual irregularity, and pain. Pregnancy is rare in the presence of genital tuberculosis and is often complicated by ectopic pregnancy or spontaneous abortion.

Clinical features of female genital tuberculosis, if any, are nonspecific and diagnosis may be difficult. A definitive diagnosis of endometrial involvement can be made using endometrial biopsy. The endometrial cavity may be obliterated by adhesions and thick synechia. In end-stage disease, the endometrial cavity may be completely obliterated.

Clinical Presentation

Renal tuberculosis may remain dormant for many years after the kidneys become seeded during the primary tuberculous infection. With reactivation, one or more renal abscess is produced. Patients usually become symptomatic, with extension of the disease to the renal pelvis and ureters causing hydronephrosis.

Specific symptoms may be lacking until the hydronephrotic kidney becomes secondarily infected.

Symptoms of frequency, urgency of urination and dysuria may ensue, with development of tuberculous cystitis. However, long before patients become symptomatic, sterile pyuria, albuminuria, and hematuria are present but cultures for organisms may demonstrate negative results.

Diagnosis is usually arrived by smear and culture of acid fast bacilli from more than three early morning urine specimens, imaging, and cystoscopy. Needle aspiration biopsy is a last resort when urine cultures are negative.

Occasionally, the treatment has to be initiated empirically with indirect evidences of genitourinary tuberculosis.

INVESTIGATIONS

Urine Examination

Urine analysis is abnormal in 90% of patients. Sterile pyuria, microscopic haematuria and acid pH are the features that should suggest the possibility of urinary tract tuberculosis.

Urine smear and culture is the most definite method for specific diagnosis of urinary tract tuberculosis. Culture of early morning specimens of urine for acid fast bacilli is the standard test that has been used most successfully for the diagnosis of genitor urinary tuberculosis.

To reduce false positive rate, multiple urine samples (more than 3 urinary samples) should be taken, as shedding of mycobacteria from the renal foci into the urine may be sporadic.

Acid Fast Bacilli (AFB) Staining

Mycobacterium tuberculosis when stained by Ziehl-Neelson Method retains its red color (Carbol fuschin) and resists decolorisation with acid alcohol. The mechanism of acid fastedness is due to formation of complexes between the dye and

mycolic acids in the cell wall resulting in trapping of the dye within the cell.

CULTURE

M.tuberculosis can be grown in pure culture and it exhibits a very slow rate of growth and multiplication by binary fusion. The doubling time is approximately 18 to 24 hours under optimal conditions. The commonest culture medium used is Lowenstein Jenson Media. It's growth in solid media as visible colonies take 3 to 4 weeks. The slow growth requires 6 to 8 weeks to achieve maximum sensitivity.

Successful attempts have been made to identify tubercle bacilli more rapidly.

1. BACTEC Method
2. Mycobacteria Growth Indicator Tube (MGIT) System
3. Luciferase Reporter Mycobacteriophage (LRM) Test

PCR (Polymerase Chain Reaction)

It is a DNA amplication method that uses specific DNA sequences to serve as markers for the presence of microorganisms. It has the potential to shorten the time required

for diagnosis from 2 to 3 weeks to 24 hours. It has 90 % sensitivity and specificity.

The Tuberculin skin test

Although far from definitive, it is an essential adjunct in diagnosis. The standard dose of 5 tuberculin units of purified protein derivative of tuberculin (PPD) in 0.1 ml of solution is injected intradermally, usually on the volar surface of the forearm.

An inflammatory reaction develops at the site and reaches a maximum between 48 to 72 hours after injection. Reaction consists of a central indurated zone surrounded by an area of erythema. It is assessed by measuring the diameter of the indurated area.

Criteria for Tuberculin positivity

1. Reaction - more than 5mm of induration
   HIV positive patients, recent contacts, and immunosuppressed patients.

2. Reaction - more than 10 mm of induration

Drug abusers,high risk groups,children younger than 4yrs.

3. Reaction - more than 15 mm of induration-

Persons with no risk factors for TB.

An induration of more than 10 mm indicates infection with M.tuberculosis but does not indicate activity of the infection.

TB patients who are quite ill may show no reaction to the skin test because of inhibiting antibodies or because so many T cells have been mobilized to the lesion and few remain to produce a significant skin reaction.

The test also may be negative in persons with HIV infection, particularly if the $CD4^+$ cell count is < 200/μL or manifestations of AIDS are present.

IMAGING STUDIES

Although positive urinary finding is necessary for the definitive diagnosis, imaging studies are essential to asses the extent and severity of involvement, to monitor the effects of treatment, and to find out the complications. Radiological

findings are widely variable, and urinary tract tuberculosis has been designated as the great imitator.

Plain X-ray KUB

- May demonstrate calcified lesions of urogenital tract involved by tuberculosis
- Irregular flecks of calcium of varying size and opacity produce an amorphous pattern
- Sometimes the calcification may outline an entire kidney, including both the parenchyma and pelvicalyseal system
- May demonstrate calcifications in the ureter and bladder in advanced cases
- Ureteral calcification in tuberculosis is different from that in Schistosomiasis, as Schistosomiasis of the ureter produces marked dilatation, and the calcification which is limited to the lower end.
- Calcification of the seminal vesicles or vas deferens is highly suggestive of tuberculosis, especially in young nondiabetic patients
- Calcification may also occur in paraspinal or psoas abscesses or abdominal and pelvic lymph nodes, and skeleton involvement may be suggestive of tuberculosis

INTRAVENOUS UROGRAPHY (IVU)

- Early findings are well demonstrated in IVU or retrograde pyelography.
- Ultrasonography,CT,and MRI do not have the spatial resolution to demonstrate minor papillary and urothelial changes that are features of early renal tuberculosis
- Late changes may be seen in US and CT. Overall,US and CT reveal findings in patients with advanced urinary tract tuberculosis similar to those described with IVU.

Findings

Findings in the kidneys

- Signs of extrarenal active or inactive tuberculosis may be apparent, such as osseous or paraspinal changes of tuberculosis and old healed calcified splenic, hepatic, lymph node, and adrenal granulomas.

- Chest radiographs may show evidence of active or healed tuberculosis in 50% of patients. The remainder have normal chest studies.
- Changes of renal tuberculosis are unilateral in 75% of patients.

- A tuberculoma usually starts as a localized caseating lesion, most commonly in the upper pole of the kidney, although it may arise anywhere.
- With time, the nidus of infection enlarges and ruptures into a neighboring calyx, discharging necrotic caseous material and distorting the calyx.
- At this stage, a variety of radiologic abnormalities may be demonstrated, including smudged papillae due to surface irregularity of the papillae, a moth-eaten calyx (early sign), irregular tract formation from the calyx to the papilla, and large irregular cavities with extensive destruction secondary to papillary necrosis.
- Changes may be detected on intravenous urography, retrograde pyelography, and on some CT and MRI scans.
- The kidney enlarges initially but subsequently may return to normal or become atrophic.
- Once communication with a tuberculous cavity is established, the involved calyx becomes an ulcerocavernous lesion.
- The finding of hydrocalyces with no pelvis dilatation or an atrophic pelvis is highly suspicious for tuberculosis. The cephalic retraction of the inferior medial margin of the

renal pelvis at the UPJ, or "the hiked up renal pelvis" may be seen urographic or pyelographic studies.

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- The infection spreads to the stem of the involved calyx, which may develop a stricture, thus sealing off the involved calyx (phantom calyx). This change may be apparent as a mass lesion.

- Dilated calyces often are associated with infundibular strictures and may be demonstrated radiologically. The lesions may be depicted better on cross-sectional imaging.
- If the ulcer or stricture extends to the renal pelvis or the pelvi ureteric junction, urine outflow obstruction may occur. In this instance, intravenous urogram may show

delayed function, clubbed calyces, or absence of function. At this stage, a "putty" kidney may be depicted. Ultrasound, CT scan, and MRI can depict an outflow obstruction.

- If tuberculous infection extends directly to the rest of the kidney, the entire kidney becomes a bag of caseous necrotic pus.
- Plain radiographs may reveal dystrophic calcification, but intravenous urography usually shows absence of function, although a faint nephrogram may be demonstrated if some amount of function remains.
- Associated renal calculi are found in as many as 20% of patients with renal tuberculosis.
- The final outcome of renal tuberculosis is autonephrectomy, which represents a small, shrunken, scarred, nonfunctioning kidney and is often associated with dystrophic calcification.

ULTRASOUND

Findings

Sonography is not as sensitive as intravenous urogram or CT scanning because of problems with identifying calyceal, pelvic, or ureteric abnormalities.

- The kidney may appear entirely normal in both early and later stages of renal tuberculosis.
- Hypoechoic/cystic masses communicating with the collecting system may be observed, representing "excluded" calyces without dilatation of the renal pelvis.
- Large abscesses may distort the renal contour and may mimic tumors or cysts.
- Usually, renal tuberculomas appear as a solid mass with diminished through transmission; however, a diffuse infiltrative type of renal tuberculosis has been described in which the kidney may appear normal on ultrasound images.
- Fibrosis and scarring may appear identical to chronic pyelonephritis or multiple renal infarcts.

Degree of Confidence

Sonographic findings may suggest genitourinary tuberculosis in the appropriate clinical setting and findings. In patients with female genital tract tuberculosis, awareness of

sonographic changes associated with the infection may improve diagnostic accuracy and avoid clinical mismanagement and surgical explorations in genital infections associated with wet-type (peritonitis) of tuberculosis.

False Positives/Negatives

Mimics of renal tuberculosis include conditions such as focal compensatory hypertrophy, focal nontuberculosis hydronephrosis, acute focal bacterial nephritis, focal or global Xanthogranulomatous pyelonephritis, BCG granulomas, and chronic pyelonephritis. Tuberculous autonephrectomy may resemble renal hydatid disease. Bladder tuberculosis may mimic bladder papilloma/transitional cell tumors. Tuberculous epididymitis may mimic other forms of chronic epididymitis /orchitis, testicular granulomas, and tumors.

Computed Tomography

Findings

While intravenous urography is the primary modality for imaging renal tuberculosis, CT scans clearly reveal changes of renal tuberculosis, particularly in advanced disease. Changes such as calcification, calyceal dilatation without a hydropelvis, parenchymal loss, and extrarenal spread are well depicted.

CT scans may demonstrate dense prostatic calcification in tuberculous prostatitis, sloughing, and irregular cavitation of the prostate, eventually resulting in a smooth-walled cavity that replaces the prostate.

Degree of Confidence

Since the type and distribution of calcification features may be suggestive of tuberculosis, CT scans (with the ability to depict calcification) may show relatively specific findings. While CT scans clearly demonstrate changes of advanced disease, sensitivity in early disease may be low because scans do not demonstrate the detailed calyceal anatomy.

False Positives/Negatives

Early disease may be missed on CT scans. Mimics of renal tuberculosis include Schistosomiasis, Diabetes Mellitus, Fungal infections, and focal papillary necrosis of other causes.

MRI

Findings

MRI is good at depicting tuberculous cavities, sinuses tracts, fistulous communications, and extrarenal and extraprostatic spread. Multiplanar MRI allows evaluation of the

disease extent in the prostatic bed and the presence of sinuses and fistulae. MRI contrast agents facilitate evaluation. MRI is also useful in the evaluation of peritonitis and adnexal masses.

Degree of Confidence

MRI is an excellent modality at depicting extra organ spread and discharging sinuses and fistulae but calcification is not readily demonstrated.

False Positives/Negatives

Sensitivity of MRI in the diagnosis of early genitourinary tract tuberculosis is low and changes of more advanced disease demonstrated on MRI scans are nonspecific.

Preferred Examination

- While intravenous urography remains the primary modality used to image patients with renal, ureteric, and bladder tuberculosis, findings of urinary tuberculosis are also detectable on ultrasound, CT scan, or MRI.
- Plain radiography may provide a clue to the diagnosis and may guide further imaging.

- Since the type and distribution of calcification may be suggestive of tuberculosis, CT scans (with the ability to depict calcification) may be helpful.
- MRI is useful when fistulae or tuberculous tracts are formed.
- Hysterosalpingography (HSG) images may suggest female genital tuberculosis by demonstrating abnormal findings within the uterus and fallopian tubes.
- Sonographic findings in the appropriate clinical setting may help to avoid orchidectomy for benign testicular disease.

Limitations of Techniques

All imaging findings may be normal in patients with early genitourinary tuberculosis. Genitourinary calcification may occur in patients with diabetes mellitus and Schistosomiasis. Brucellosis also may mimic tuberculosis. The differential diagnosis of an adnexal mass is wide.

A congenital megacalyx and focal papillary necrosis may mimic renal tuberculosis radiologically. Papillary necrosis can result from Diabetes,analgesic abuse and tuberculosis. A

tuberculous testicular granuloma may mimic a testicular neoplasm on ultrasound images.

Small areas of calcification are difficult to detect on MRI scans although they are pivotal to the diagnosis of tuberculosis. HSG findings are also nonspecific; blockage of the fallopian tubes is not pathognomonic for tuberculous salpingitis and may occur as a result of other forms of infective processes of the genital tract.

Findings in all imaging modalities used in the diagnosis of genitourinary tuberculosis are essentially nonspecific because the diagnosis is based on the presence of calcification, cavities, and strictures, which are associated with a long list of differential diagnosis.

Medical management

GUTB responds better to a short course of treatment than pulmonary TB, because it carries a lower mycobacterial load.Isonicotinic acid hydrazide (INH) and Rifampicin penetrate well into the cavitary lesions associated with GUTB. A high concentration of INH, Rifampicin, and Pyrazinamide are maintained in urine.

- The primary aims of treatment are to preserve renal parenchyma and function, to make the patient noninfectious, and to manage comorbid conditions.
- Monitor culture and sensitivity reports, and change the regimen if necessary.
- Standard treatment is Rifampicin, INH, pyrazinamide, and Ethambutol for 2 months, then Rifampicin and INH for 4 more months unless resistance to either agent exists. If resistance exists, obtain a follow-up sensitivity report.
- In patients who are HIV positive, continue treatment for a total of 9 months.

Examples of short course therapy are as follows:

  - Prescribe 2 months of daily therapy with INH, Rifampicin, and Pyrazinamide, then 2 months at 3 times a week with INH and Rifampicin.
  - Prescribe 4 months of therapy at 3 times a week with INH, Rifampicin, and Pyrazinamide. This course is cost-effective in developing countries if compliance is assured, although it may promote multidrug resistance.

- Indications for prescribing steroids include the following:

- Severe bladder symptoms
- Tubular structure involvement (e.g., ureter, fallopian tubes, spermatic cord) in early stages.

- High-dose prednisone (ie, at least 20 mg tid) for 4-6 weeks is recommended because Rifampicin reduces effectiveness and bioavailability of prednisone by 66%.

Directly Observed Treatment, Short Course (DOTS) Chemotherapy

DOTS is a strategy to ensure cure by providing the effective medicine and confirming that it is taken. It is the only strategy which has been documented to be effective worldwide on a programme basis.

In DOTS, during the intensive phase of treatment, a health worker or other trained person watches as the patient swallows the drug in his presence.

During continuation phase, the patient is issued medicine for one week in a multiblister combipack, of which the first dose is swallowed by the patient in the presence of health worker or trained person.

The consumption of medicine in the continuation phase is also checked by return of empty multiblister combipack, when the patient comes to collect medicine for the next week. The drugs are provided in patient-wise boxes with sufficient shelf-life. In this program alternate day treatment is used.

The cases are divided into three types of categories

Category-I - New sputum smear positive
Seriously ill extra-pulmonary
(Genitourinary tuberculosis)

Category-II - Sputum positive relapse
Sputum positive –failure
Sputum positive after default

Category-III - Sputum negative, not seriously ill
Extrapulmonary,not seriously ill

Isoniazid (INH)

- First-line agent for susceptible mycobacteria
- Bactericidal or bacteriostatic, depending on concentration and susceptibility.
- More effective, less toxic, and less expensive

- Inhibits mycolic acid synthesis necessary for mycobacterial cell wall formation. Affects mycobacterial MAO and diamine oxidase.

Adverse effects - include peripheral neuropathy, optic neuritis, encephalopathy, hepatitis, interstitial nephritis, gynecomastia, lupus like syndromes, anemia.

Adult Dose - 5 mg/kg/d PO (usual daily dose - 300 mg)

Contraindications - Documented hypersensitivity, hepatic disease,alcoholism.

Precautions – To be taken in empty stomach**,** Obtain baseline LFT, stop if aminotransferase level triples; in lactating mother, watch for neurotoxicity or hepatotoxicity in child; supplement pyridoxine to avoid neurotoxicity; toxic dose is more than 20 mg/kg/d; studies show that even in anuric patient, dosage of 300mg (5 mg/kg)is well tolerated.

Rifampicin

- First-line agent
- Bactericidal and bacteriostatic, depending on concentration and susceptibility.

- Binds to beta subunit of DNA-dependent RNA polymerase and inhibits bacterial RNA synthesis
- Effective against both slowly and actively dividing bacteria in both cavitary and caseous lesions

Adverse effects - include hepatitis, interstitial nephritis, hemolysis,glomerulonephritis, nephrotic syndrome, pancreatitis, pseudomembranous colitis, myopathy, pruritus, and discoloration of body fluids.

Adult Dose - 10 mg/kg/d PO; not to exceed 600 mg/d

Contraindications - Documented hypersensitivity, hepatic disease, alcoholism.

Precautions – To be taken on empty stomach, in renal insufficiency- no need to lower dose below 600 mg/d (leads to significant reduction in effectiveness); in hepatic impairment, dose should not exceed 8 mg/kg/d; obtain periodic LFT; decreases effectiveness of oral contraceptives and additional measures should be used for at least 1 cycle after course of rifampicin; lowers serum concentration of protease inhibitors and nonnucleoside reverse transcriptase inhibitors.

Pyrazinamide

- First-line drug.
- Bactericidal or bacteriostatic, depending on concentration and susceptibility
- Less toxic, more effective
- Effective against only *M tuberculosis*

Adverse effects - include hepatitis, hyperuricemia, photosensitivity, sideroblastic anemia, thrombocytopenia.

Adult Dose - 15-30 mg/kg/d PO; not to exceed 2 g/d

Contraindications - Documented hypersensitivity; hepatic disease, gout; alcoholism

Precautions - Use only in combination with other effective antituberculous agents; inhibits renal excretion of urates; may result in hyperuricemia (usually asymptomatic); perform baseline serum uric acid determinations; discontinue if signs of hyperuricemia with acute gouty arthritis appear; perform baseline LFTs (closely monitor in liver disease); discontinue pyrazinamide if signs of hepatocellular damage appear. In renal impairment adjust dose as follows:

- Creatinine Clearence >50 mL/min - No dosage adjustment.

- Creatinine Clearence 10-50 mL/min - Extend dosing interval to 48-72 h
- Creatinine Clearence <10 mL/min - Extend dosing interval to 72 h
- In patient on dialysis administer dose 24 h before dialysis.
- Monitor the serum uric acid level.

Ethambutol

- Second-line treatment
- Bactericidal and bacteriostatic, depending on concentration
- Inhibits RNA synthesis

Adverse effects - include optic neuritis, peripheral neuropathy, hyperuricemia, fever, thrombocytopenia, proteinuria, interstitial nephritis, arthralgia, and toxic epidermal necrolysis.

Adult Dose - 15-25 mg/kg/d PO; not to exceed 1600 mg/d

Contraindications Documented hypersensitivity, ocular disease, gout and renal disease

Precautions : Reduce dose in patients with impaired renal function. Visual adverse effects may be reversible if promptly discontinued.

Streptomycin

- Second- or third-line treatment
- Bactericidal by inhibiting protein synthesis through irreversible binding to 30S ribosomal subunit in susceptible bacteria

Adverse effects - include ototoxicity, renal tubular acidosis, renal tubular necrosis, myasthenia, exfoliative dermatitis.

Adult Dose - 15 mg/kg/d IM (deep); not to exceed 1 g/d; alternatively, 25-30 mg/dose 3 times/wk IM (deep)

Contraindications Documented hypersensitivity; hepatic or renal impairment.

Precautions - not intended for long-term therapy, caution in renal failure not on dialysis ; In renal impairment, adjust dose as follows:

- Creatinine Clearance > 80 mL/min - No dose adjustment
- Creatinine Clearance - 50-80 mL/min - Reduce dose to 7.5 mg/kg/d

- Creatinine Clearance - 10-49 mL/min - Reduce dose to 7.5 mg/kg 1-3d.
- Creatinine Clearance <10 mL/min - Reduce dose to 7.5 mg/kg once in 3-4d.

Surgical treatment

Although chemotherapy is the mainstay of treatment, surgical intervention, either as ablation or reconstruction, is often required during the course of GUTB. Generally, at least 4-6 weeks of chemotherapy with appropriate agents is first administered if immediate surgery is not necessary.

- Indications for surgery
  - Hydronephrosis
  - Progressive renal insufficiency secondary to obstruction
  - Nonfunctioning or poorly functioning kidneys
  - Reduced bladder capacity

- Ablative surgery
  - Partial or total Nephrectomy
  - Nephroureterectomy
  - Epididymectomy

- Reconstructive surgery
    - DJ Stenting
    - Ureteric dilatation and ureterostomy
    - Replacement or reimplantation of ureter
    - Urinary diversion
    - Augmentation cystoplasty

Follow-up

- A urologist should provide constant follow-up care in order to prevent further irreversible parenchymal damage.
- Patients should be seen 3,6,and 12 months after course of chemotherapy has finished.
- At each review, three consecutive early morning specimens of urine are examined and an intravenous urogram is performed.
- If radiographic results remain unchanged and the urine is consistently sterile, the patient is discharged with instructions to report back if there is any recurrence of previous urinary symptoms.

Diet:

- Institute a high-nutrition diet for malnourished patients.

Activity:

- GUTB can be sexually transmitted until mycobacterial excretion ceases.

MATERIALS AND METHODS

Over a period of 3 years from June 2003 to August 2005, in Our Department of Urology, Government Royapettah Hospital & Kilpauk Medical College Hospital, we have received and treated 46 cases of genitourinary tuberculosis coming from various parts of Tamil Nadu and Andra Pradesh.

Patients suspected to have Genitourinary Tuberculosis were investigated with following investigations,

1. Haematocrit.

2. Total and Differential WBC Count.

3. ESR.

4. Urine investigations like albumin,sugar,deposits.

5. Three days preferably five early morning urine for AFB-smear and culture

6. Renal parameters.

7. Ultrasound KUB.

8. Intravenous Urogram.

9. X-ray Chest.

10. Endoscopy and if necessary biopsy.

11. Antegrade studies in relevant cases.

Patients diagnosed with Genitourinary tuberculosis were analysed into

1. Percentage of patients with ureteric involvement

2. Male, Female sex ratio

3. Presentation in various age group

4. Various modes of clinical presentation

5. Investigations

6. Level of stricture involvement in the ureter

7. Urgent treatments like DJ Stenting or PCN

8. Medical management alone

9. Medical management with various surgical management

10. Role of our management in salvaging the kidney function.

Patients were classified into those presenting with obstructive uropathy and without obstruction. Those presenting bladder involvement without obstructive uropathy were investigated and Antituberculous drug treatment was started.

During Cystoscopy random bladder biopsy was taken and sent for histopathological examination.

Patients presenting with obstructive uropathy with functioning renal parenchyma were submitted for Cystoscopy under anaesthesia and DJ Stenting was attempted on the affected side. If stenting was done patient was continued with antituberculous treatment and DJ stent was changed once in 3 months.

After 6 months DJ stent was removed and IVU was done to asses the renal function and obstruction. If function was alright patients were followed regularly. If there is obstruction DJ Stenting was done again.

If Stenting was not possible,percutaneous nephrostomy was performed.PCN fluid was analysed including the volume and

qualitative analysis.If the kidney was salvageable,surgical procedures like Ureteroneocystostomy or Boari's flap were done.

If the kidney is poorly functioning Nephroureterectomy was done. If there is lower ureteric stricture associated with reduced bladder capacity, Augmentation Cystoplasty with ureteric reimplantation into bowel segment was done.

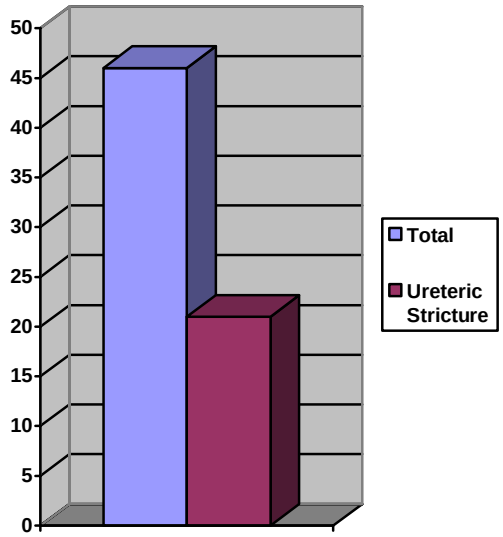
One patient had bilateral urinary tuberculosis-with left nonfunctioningkidney, multiple right ureteric stricture with renal failure. Emergency Percutaneous nephrostomy was done on the right side, but patient did not want to take further management and patient was followed with regular PCN catheter change.

OBSERVATION

In this prospective study,over a period of 3 years from June-2003 to August-2005,cases diagnosed as GUTB were analysed

Total number of cases of GUTB - 46 (54.3%)

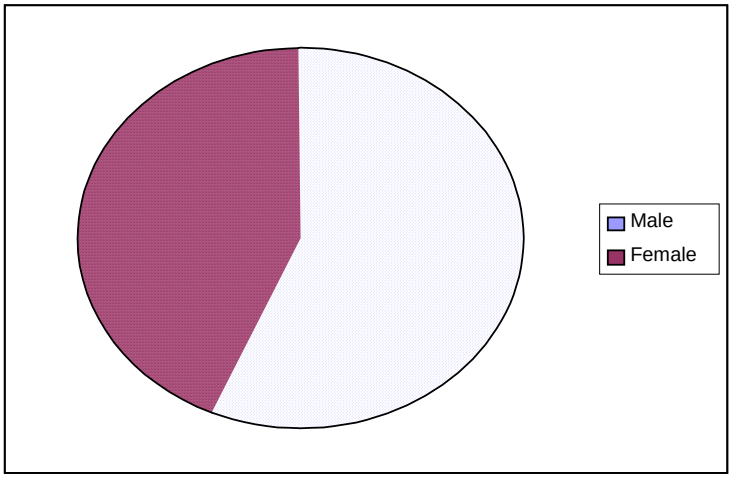
Ureteric Stricture cases in GUTB - 21 (45.7%)



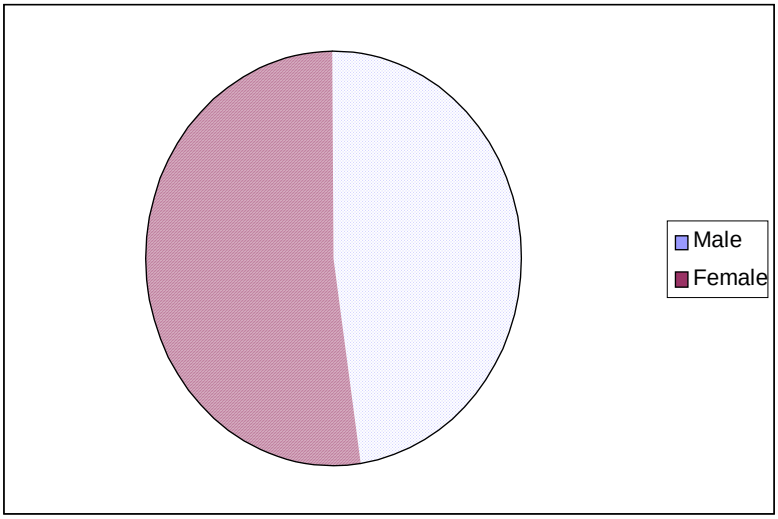
SEX DIFFERENCE

	Genitourinary tuberculosis	Ureteric Stricture
Male	26	10
Female	20	11

Genitourinary tuberculosis

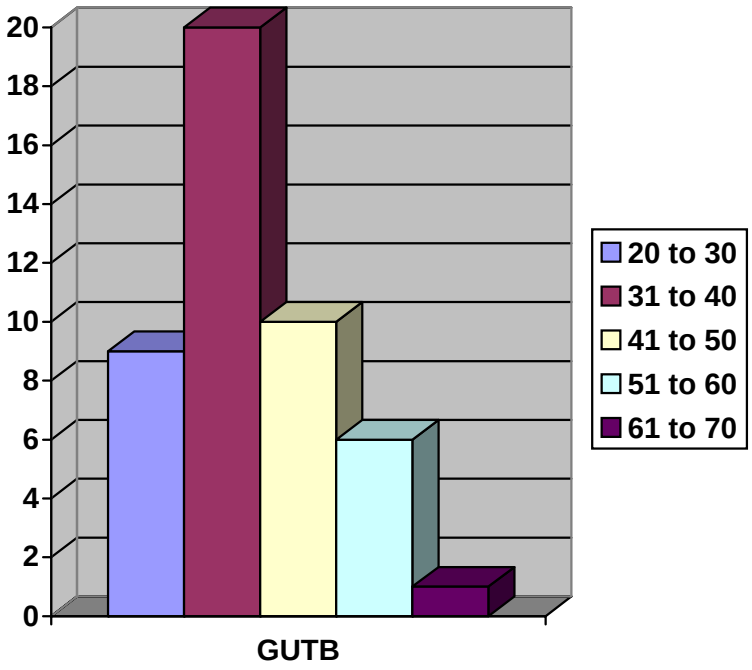


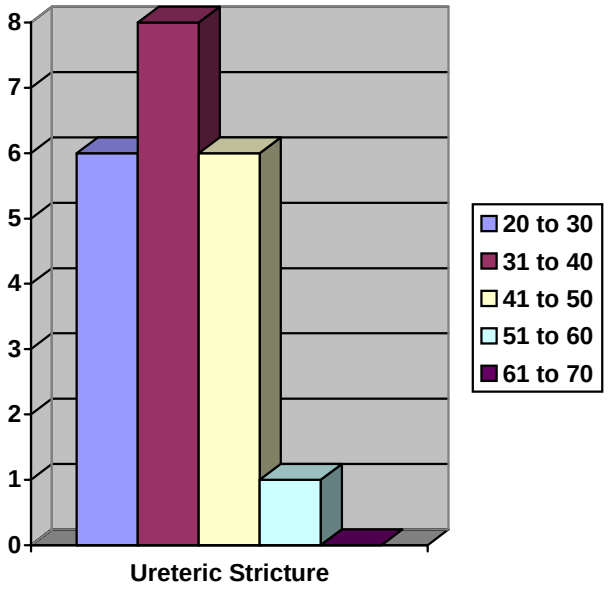
Ureteric Stricture due to GUTB



AGE DISTRIBUTION

Age in years	Genitourinary tuberculosis	Ureteric Stricture
20 to 30	9	6
31 to 40	20	8
41 to 50	10	6
51 to 60	6	1
61 to 70	1	0





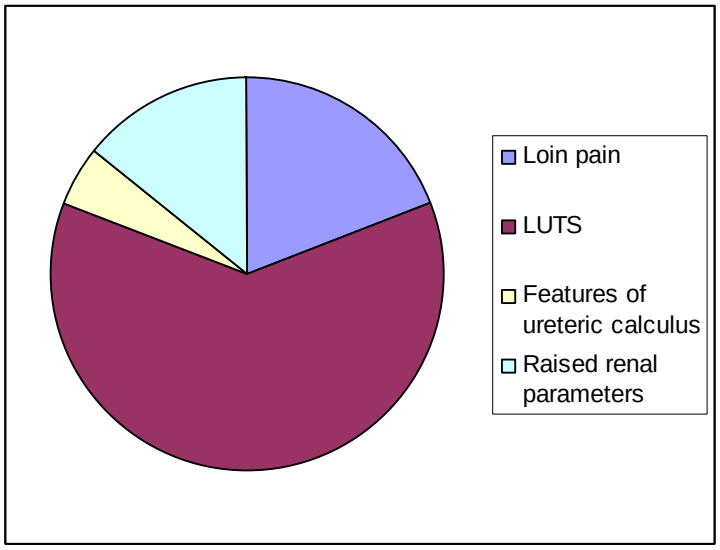
CLINICAL PRESENTATION

1.Loin pain - 4 cases

2.LUTS - 13 case

3.Presented with features of ureteric stone - 1 case

4.Raised renal parameters - 3 cases



INVESTIGATIONS

S.No	Investigation	No.of Cases
1.	Urine for AFB smear	3
2.	Urine for AFB Culture	4
3.	Diagnosed by bladder biopsy	4
4.	Post operative diagnosis by biopsy	5
5.	Empirical diagnosis	6

URETERIC STRICTURE-SIDE

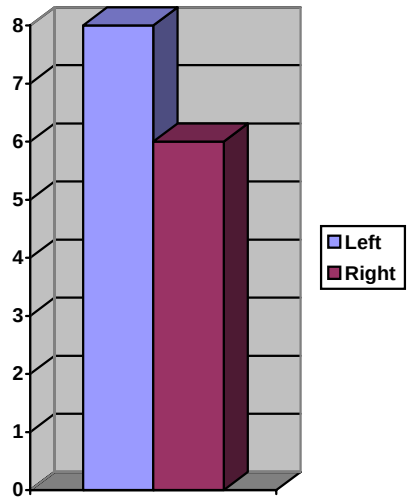
Total number of cases - 21 cases (45.7%)

Unilateral strictures - 14 cases (66.7 %)

Bilateral stricture - 7 case (33.3 %)

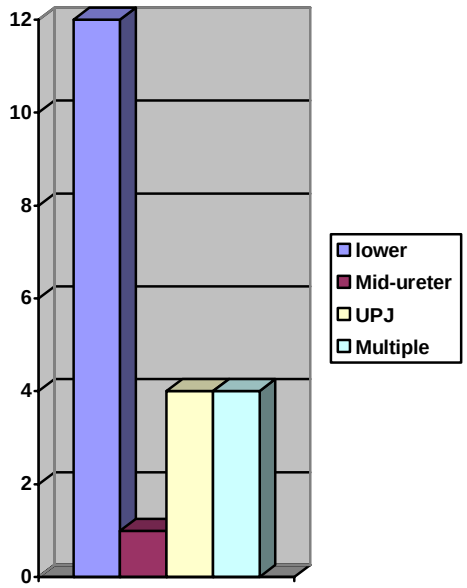
1. Left unilateral stricture - 8 cases (57.1%)

2. Right unilateral stricture - 6 cases (42.9%)



URETERIC STRICTURE-SITE

Lower ureteric stricture	-	12 cases	(57.2%)
Mid-ureteric stricture	-	1 case	(4.8%)
UPJ stricture	-	4 cases	(19%)
Multiple stricture	-	4 cases	(19%)

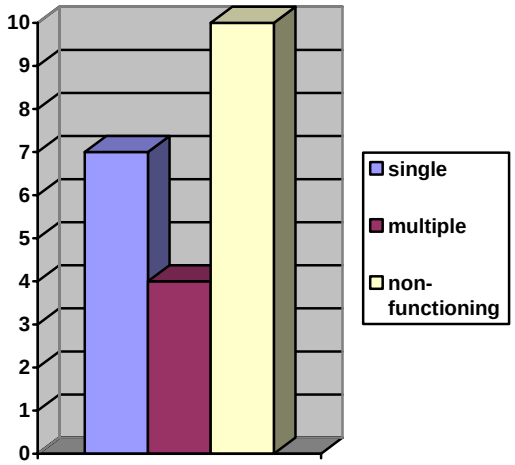


SEVERITY

1. Multiple stricture - 4 cases (19.0%)

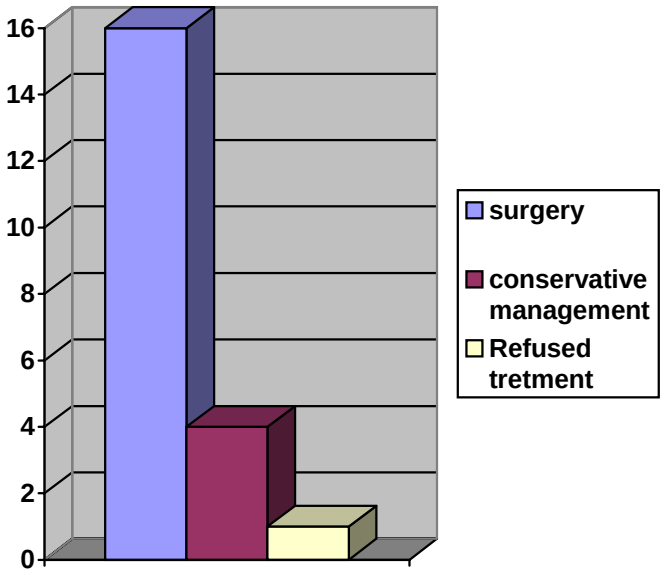
2. Ureteric stricture with ipsilateral renal function deterioration - 10 cases (47.6%)

3. Single ureteric stricture - 7 cases (33.3 %)



MANAGEMENT

- Surgery - 16 cases (76.2%)
- Conservative management - 4 cases (19.0 %)
- Refused treatment - 1 case (4.8 %)

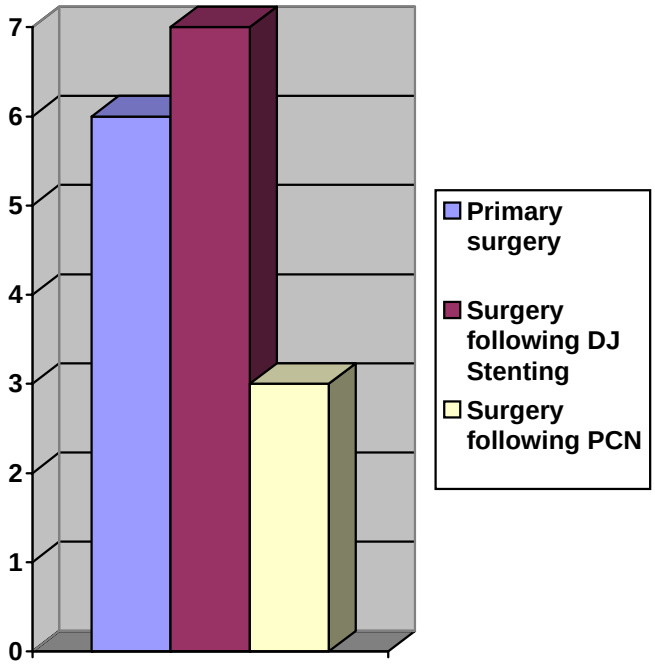


SURGERY

Primary surgery - 6 cases (37.5%)

Surgery following DJ Stenting – 7 cases (43.8%)

Surgery following PCN – 3 cases (18.7 %)



SURGICAL PROCEDURES

- Nephrectomy -11 cases (55.5 %)
- Vesico-ureteric reimplantation alone - 2 cases (11.1%) (Extravesical reimplantation)
- Boari's flap - 1 case (5.5 %)
- Augmentation cystoplasty with ureteric reimplantation - 2 cases (11.1%)

Primary surgery

Nephrectomy

Nephrectomy was performed for 6 cases. 5 cases were diagnosed preoperatively as nonfunctioning units due to Tuberculosis and underwent Nephrectomy after 6 weeks course of Antituberculous drugs.

One case was diagnosed as ureteric calculous with nonvisualised system due to obstruction,planned for ureterolithotomy.On exploration whole ureter was fibrotic,and biosy came as tuberculous ureteritis and subsequently Nephrouretectomy was performed.

Surgery following DJ Stenting

Primary DJ Stenting was performed and antituberculous treatment was given for 7 cases for 6 months.

After removal of the stent the renal units did not regain function at all and hence Nephrectomy was performed.

Surgery following Percutaneous Nephrostomy

Percutaneous nephrostomy was performed for 2 patients with ureteric obstruction where DJ Stenting could be performed. Percutaneous Nephrostomy was not drainig adequately because of poor function and hence Nephrectomy was performed.

One case had bilateral involvement with nonfunctioning left kidney, lower ureteric obstruction producing hydroureteronephrosis on right side with thimble bladder, Emergency right percutaneous nephrostomy was done and subsequently left nephroureterectomy, augmentation cystoplasty with right ureteric reimplantation into bladder was done.

DISCUSSION

Over a period of 3 years, cases diagnosed with genitourinary tuberculosis were analysed as a prospective study.

The ureteric stricture in relation to cases of genitourinary tuberculosis

- In this series 45.7% (2003 - 2005)
- In Hy' series: 28.7% (1989 – 1994)
- In Gow' series: 9% (1994)

In comparison with those of Western authors, our incidence is much higher, and the trend is rising despite the improvement of socio-economic conditions and living standards in recent years .

Genitourinary tuberculosis commonly affects male population, and this study male predominance is 56.5 % for GUTB and 47.6% for the ureteric stricture due to GUTB.

Commonly it affects the age group of 20 to 40 years. In this series about 63.0% for GUTB and 66.7 % for ureteric stricture patients were from the age group of 20 to 40 years.

The clinical manifestations of the disease are still complicated with bilateral lesions (33.3%). Multiple strictures (19%), and ureteric stricture with ipsilateral renal function deterioration (47.6%).

Ureteric stricture was common on the left side (57.1%). Lower ureter was the commonest area of affected by the stricture (57.2 %). Multiple strictures occurred in 19 % of patients.

Surgery was the main mode of treatment (76.2%) since the cases were presented in a advanced stage. Nephrectomy was performed for 55.5 % patients in spite of our measures to save renal unit.

Despite our recent efforts of applying the interventional endoscopy and refining the surgical skills and techniques, our ultimate outcome rests unsatisfactory:

CONCLUSIONS

The complication of tuberculous ureteric stricture in this population remains common and complicated. The incidence is still very high. The clinical manifestations are polymorphous, and the renal function deterioration rate is quite high.

The accurate assessment is sometimes difficult because of nonvisualised system in IVU. However, a fairly confident diagnosis can be made in most instances with clinical correlation.

Despite our recent efforts of supervising the patients and refining the treatment modalities, including the interventional endoscopy, our overall outcome of treatment appears modest and unsatisfactory.

The socio-economic conditions may play an important role in final outcome. Genitourinary tuberculosis is a manifestation of systemic tuberculosis. The anti-tuberculous campaigns of the society need emphasis.

Beware of the WHO's warning: the tuberculosis is returning.

IN SUMMARY

- Symptoms non-specific, high index of suspicion needed
- Diagnosis difficult & delayed

1. Imaging changes are observed late in the disease,
2. In many instances, significant group have many differential diagnosis,

3. And the diagnosis is determined by culture, not imaging.

- Supervised, short course intensive combination chemotherapy
- Individualised management & follow-up

REFERENCES

1. World Health Organization - WHO Report on the Tuberculosis Epidemic 1996, Geneva: WHO 1996.
2. Narayana A. Overview of renal tuberculosis. Urology 1982: 19: 232.
3. Flechner SM, Gow JG. Role of nephrectomy in the treatment of non- functioning or very poorly functioning unilateral tuberculous kidney. J Urol 1980:123:822.
4. Amaresan MS, Balasingh SH. Profile, peculiarities, diagnostic puzzles in renal tuberculosis in South India (study of 75 cases). Proceedings of scientific session of Southern Chapter of Indian Society of Nephrology 1985. Daniel TM. Tuberculosis in Isselbacher KJ, Braunwald E, Wilson JD (eds): Harrison's Principles of Internal medicine, ed 13. McGraw Hill Inc. 1994, 710-718.
5. O' Flgnn G D. Surgical treatment of genitourinary tuberculosis. Br. J Urol 1970; 42:667.
6. Allen FJ, De Kock ML. Genitourinary tuberculosis - experience with 52 urology patients. *South African Medical Journal* 1993; **83:** 903-7.

7. O'Flynn JD. Surgical treatment of genitourinary tuberculosis. *British Journal of Urology* 1970; **42:** 667.

8. Calridge M. Ureteric obstruction in tuberculosis. *British Journal of Urology 1970: **42:** 688-92.*

9. Waller RM, Finnerty DP, Casarella WJ. Transluminal balloon dilation of tuberculous ureteric stricture. *Journal of Urology 1983; **129:** 1225-6.*

10. Rees RWM. The ureter in renal tuberculosis. *British Journal of Uroloay* 1970; **42:** 693-6.

11. Gow JG, Barbosa S. Genitourinary tuberculosis. A sudy of 1117 cases over a period of 34 years. *British Journal of Urology 1986; **56:** 449-55.*

12. Chung JJ, Kim MJ, Lee T, Yoo HS, Lee JT. Sonographic findings in tuberculous epididymitis and epididymo-orchitis. J Clin Ultrasound 1997; 25:390-394.

13. Das KM, Indudhara R, Vaidyanathan S. Sonographic features of genitourinary tuberculosis. AJR Am J Roentgenol 1992; 158:327-329

14. Wang LJ, Wong YC, Chen CJ, Lim KE. CT features of genitourinary tuberculosis. J Comput Assist Tomogr 1997; 21:254-258

15. Hopewell PC. A clinical view of tuberculosis. Radiol Clin North Am 1995; 33:641-653.

16. Gow J. G: Genitourinary tuberculosis. Campbell's Urology , 6th ed. , 992, vol I, pp 951- 980.

17. Gow J. G.: Genitourinary tuberculosis. Campbell's Urology , 7th ed. , 1998, Vol 1, pp 807-836.

18. Gow J. G.: Genitourinary tuberculosis. Current Urologic Therapy 3, WB Saunders, 1994, pp 57 - 59.

19. Grosset J.: Bacteriologic basis of short course chemotherapy for tuberculosis. Clin. Chest. Med. 1980, 1 , 231.

20. Harry P.Koo,David A. Bloom: Lower ureteral reconstruction. Urologic clinics of North America. Vol 26, No 1, 1999, pp167-73.

21. Tanago E. A.: Specific infections of the genitourinary tract. Smith's general Urology, 15th ed. , 2000 , p. 265.

22. Campbell's Urology-Seventh and Eighth Edition

23. Adult and Pediatric Urology-Fourth Edition-Jay Y.Gillenwater.

24. Clinical Urography-Second Edition-Howard M.Pollack.

25. Medline & Internet Searches